REMARKS

Claims 1-31 were in the application as filed. Claims 32-34 were added in the Preliminary Amendment filed on January 9, 2002. Claims 2-15, 19-30, and 32-34 were cancelled by the amendments filed on April 29, 2004.

Claim 17 has been cancelled and Claim 31 has been amended to delete its dependency from claim 17. Applicants reserve the right to prosecute the deleted subject matter in a continuing application.

Claim 18 has been amended in order to write this claim in independent form and to incorporate all of the limitations of now canceled claim 17 (from which claim 18 originally depended) into claim 18.

Claim 1 has been amended to correct an obvious typographical error.

Claims 1, 16, 18 and 31 remain in the application.

Claims 1 and 16 are objected to for the stated reason that the word "or" after "with" and before "optically active organic acids" in claim 1 is unnecessary and confusing. The Examiner indicates that the word "or" should be removed from claim 1.

In view of the deletion of the word "or" in claim 1, this objection is believed overcome and withdrawal thereof is respectfully requested.

Claims 17 and 31 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,780,466. In support of this rejection, the Examiner has stated that:

> [A]pplicant argues that the compounds of examples 68-70 of U.S. patent No. 5,780,466 are not prepared by the resolution of 2-(3,4-dichlorophenyl)-2-(2-hydroxyethyl)morpholine or any other 2-hydroxyethyl morpholine derivative of the formula II with an optically active acid as has been suggested by the Examiner but are prepared by resolution of a compound of the formula XXVII. Furthermore, applicant argues that although the disclosure of US Patent No 5,780,466 concerns the compounds of the formula II in an enantiomerically pure form or in a racemic form, nowhere in the extensive disclosure of the patent is there any specific disclosure concerning the actual resolution of a compound of the formula II or the use of such a compound as an intermediate to prepare enantiomerically pure tachykinin receptor antagonist compounds. These arguments are not found persuasive since the instant claims are drawn to applicants instant compound of the formula I in an enantiomerically pure form with an optically active organic acid and since the prior art reference does disclose the compounds of the formula (II), specifically the compounds of the formula II as found in preparations 1.5 and 1.11 which are racemic mixtures of the applicants instantly claimed

> compound, and since the prior art discloses on column 23, lines 30-37 that the enantiomers of the compounds of the formula (II) are included in the invention and since column 47, lines 34-43 disclose that the compounds of the formula (II) wherein A is –O-CH2-CH2 and E is H can be resolved into the specific enantiomers by resolving with an optically active acid, for example with (+) or (-) tartaric acid by known methods, this disclosure, of which, therefore renders obvious applicants instantly claimed compounds.

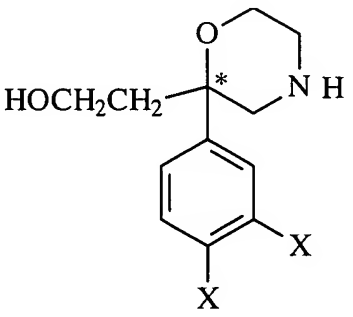
This rejection is rendered moot and should be withdrawn in view of the cancellation of claim 17 and the amendment to claim 31 deleting its dependency from cancelled claim 17.

Claim 18 is rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,780,466 as applied to claims 17 and 31 above, and further in view of U.S. Patent No. 5,616,777. In support of this rejection, the Examiner has stated that:

> In regards to the combination rejection applicant argues that US Patent No. 5,616577 does not cure applicants asserted inadequacy of US Patent No. 5,780,466 since applicants claimed compounds differ significantly structurally from the chiral hydrazines disclosed in US Patent No. 5,616,777 and it is therefore not seen how the use of chiral acids such as L-DTTA and D-DTTA to resolve such structurally different chiral hydrazines could teach the compounds of the instant claims. This argument is not found persuasive since the secondary reference of US Patent NO. 5,616,577 was used to show the common knowledge in the resolution of racemic mixtures with optically active organic acids.

This rejection is traversed and reconsideration and withdrawal thereof are requested for the reasons given hereinbelow.

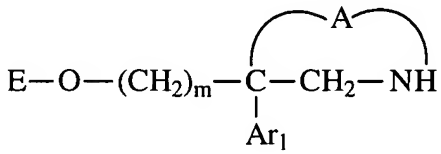
Applicants' instantly claimed compounds are directed to enantiomerically pure compounds of the Formula I:



I

in which X represents a halogen atom, in the form of an optically active salt with L-(-)- or D-(+)-di-para-toluoyltartaric acid.

Emonds-Alt et al., U.S. Patent No. 5,780,466, issued July 14, 1998, has a disclosure concerning the compounds of the formula II:



II

in enantiomerically pure form or in racemic form. However, nowhere in the extensive disclosure of this patent is there any specific disclosure concerning the actual resolution of a compound of formula II, let alone the use of such a compound as an intermediate to prepare enantiomerically pure tachykinin receptor antagonist compounds. Moreover, the groups A and Ar_1 of formula II can represent a vast array of possible substituents, and it is not seen how such a vast disclosure could possibly teach or suggest to one of ordinary skill in the art to select out the instant compounds in racemic form let alone in enantiomerically pure form, and actually teach away from the use of the compounds of Formula (I) as intermediates by teaching that such compounds are obtained in very low yields of 1% to 2%. The Examiner, though, is not persuaded that Emonds-Alt et al. actually teach away from the use of the compounds of Formula I for the stated reason that the instant claims are drawn to the compounds themselves and not to methods of use. However, the only possible motivation to prepare any intermediate compound disclosed by Emonds-Alt et al. would be for their use in a process of preparing the tachykinin receptor antagonist compounds. Since the intermediate compounds are obtained in very low yields of 1% to 2%, one skilled in the art would not be motivated to use them in a process to obtain the tachykinin receptor antagonists, and, consequently, would not be motivated to prepare them.

Finally, the Examiner acknowledges that the primary Emonds-Alt reference fails to disclose the optically active organic acids of L-(-)- or D-(+)-di-para-toluoyltartaric acid, required by the instantly rejected claims, so the secondary Andrews et al. reference, U.S. Patent No. 5,616,777, is relied upon for allegedly disclosing "chiral acids" which are used to resolve a mixture of diastereomers, with preferences towards L-DTTA and D-DTTA. As pointed out hereinbelow, the secondary reference fails to cure the inadequacy of the primary reference.

Andrews et al. disclose chiral hydrazine derivatives which are stated to be useful as intermediates in the synthesis of tri-substituted tetrahydrofuran triazole derivatives which are stated to be useful as antifungal agents. Also disclosed is a process for preparing such chiral hydrazines by resolution with chiral acids. Andrews specifically defines a "chiral acid" as "a single stereoisomer of a chiral acid which can be used to resolve a mixture of diastereomeric substituted *hydrazines*" (column, 5, emphasis added). Disclosed as preferred chiral acids for resolving a mixture of diastereomeric substituted *hydrazines* are L-DBTA, D-DBTA, L-DTTA and D-DTTA. Nowhere in Andrews is there a teaching or suggestion that the disclosed chiral acids would be useful for resolving racemic mixtures in general, such as the compounds described by Emonds-Alt et al., which are not, in fact, hydrazines. Thus, the requisite motivation to combine the cited references is clearly lacking. The Examiner's contention that Andrews shows that it is common knowledge to use the optically active acids taught by Andrews to resolve racemic mixtures generally is specifically traversed, since Andrews merely teaches the chiral acids described therein are useful for resolving diastereomeric hydrazines. Therefore, one skilled in the art would not be motivated to prepare an optically active salt of a compound of formula (I) with any of the "chiral salts" described by Andrews.

The Examiner has essentially collected references that teach various elements of the claimed invention, but has failed to properly combine the references so as to make out a *prima facie* case of obviousness. One of ordinary skill in the art would not be motivated to modify either of the cited Emonds-Alt et al. or Andrews et al. reference so as to obtain the claimed invention. The only suggestion to combine the individual elements alleged to be taught in the prior art comes from the teachings contained in Applicants' own disclosure of the invention. A collection of teachings from assorted references of individual claim elements without more does not establish a *prima facie* case of obviousness. Therefore, the claimed invention would not have been obvious to a person skilled in the art at the time the invention was made and, hence, the rejection of claims 18 and 31 based on Emonds-Alt et al. in view of Andrews et al. is believed to be unwarranted and should be withdrawn.

In view of the foregoing amendments and remarks, reconsideration and withdrawal of (a) the objection to claims 1 and 16, and (b) the rejection of claims 17, 18 and 31 under 35 U.S.C. § 103(a) is requested and allowance of claims 1, 16, 18, and 31 is respectfully requested.

Respectfully submitted,

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